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Attenuated vaccines as model respiratory viral infection systems: from human to bovine

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Background
In both humans and livestock, viral-bacterial interactions in the upper respiratory tract (URT) appear to be important for development of respiratory disease. In healthy pre-school children, density of commensal nasopharyngeal bacteria has been demonstrated to increase following live-attenuated influenza vaccine. Dysbiosis of respiratory microbiota may influence transmission dynamics.

Objectives
To investigate carriage of *Pasteurellaceae* in the bovine URT and whether carriage density increases following mild respiratory viral infection.

Methods
Two cohorts of healthy beef suckler calves were bred, and housed post-weaning in three identical barns at the BBSRC National Capability, North Wyke Farm Platform (BBSRC, BB/J004308) over two successive years. We evaluated baseline carriage and density of *Pasteurellaceae* in calves born in 2015 (n = 60) and the effects of respiratory viral infection on *Pasteurellaceae* colonisation in calves born in 2016 (n = 87); using a stepped wedge design double-blind cluster randomised trial. Calf clusters (n = 29) received intranasal live-attenuated vaccine (RS+PI3) or placebo. Nasal swabs and jugular blood were collected from calves. Three qPCR assays were developed to detect and quantify *Pasteurella multocida*, *Mannheimia haemolytica* and *Histophilus somni*.

Results
The stepped wedge cluster-randomised trial will be described. Baseline rates of carriage were higher for *P. multocida* (57/60; $CI_{95\%}$: 0.852 – 0.987 and 72/87; $CI_{95\%}$: 0.728 – 0.897) than for *H. somni* (30/60; $CI_{95\%}$: 0.370 – 0.630 and 36/87; $CI_{95\%}$: 0.311 – 0.524) in both years. In absence of vaccination, carriage for both species decreased over time. Density of *P. multocida* carriage at baseline ranged widely over 5 orders of magnitude.

Conclusion
We have developed methods for rapid detection and quantification of *Pasteurellaceae* from nasal swabs, and demonstrated their usefulness in investigating pathogen colonisation of the bovine URT. We are currently using these methods together with attenuated vaccine viruses as tools to explore respiratory host-microbiome interactions in cattle.